

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 August 2000 (24.08.2000)

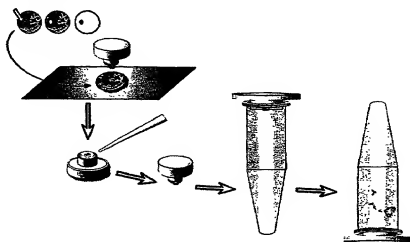
PCT

(10) International Publication Number
WO 00/49410 A3

- (51) International Patent Classification⁷: G01N 33/68, 1/30, B01L 3/00
- (21) International Application Number: PCT/US00/04023
- (22) International Filing Date: 16 February 2000 (16.02.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/120,288 16 February 1999 (16.02.1999) US
- (71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY DEPARTMENT OF HEALTH & HUMAN SERVICES, THE NATIONAL INSTITUTES OF HEALTH [US/US]; Office of Technology Transfer, 6011 Executive Boulevard, Suite #325, Rockville, MD 20852 (US).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): LIOTTA, Lance, A. [US/US]; 8601 Bradley Boulevard, Bethesda, MD 20817 (US). SIMONE, Nicole [US/US]; 16 Balsam Court, Lawrenceville, NJ 08648 (US). EMMERT-BUCK, Michael [US/US]; 13620 Cedar Creek Lane, Silver Spring, MD 20904 (US). PETRICIOIN, Emmanuel, E., III [US/US]; 2805 Feather Ridge Court, Dunkirk, MD 20754 (US).
- (74) Agent: NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Winston, Leigh, Suite 1600 - One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

[Continued on next page]

(54) Title: LCM (LASER CAPTURE MICRODISSECTION) FOR CELLULAR PROTEIN ANALYSIS



(57) Abstract: The present invention describes devices and methods for performing protein analysis on laser capture microdissected cells, which permits proteomic analysis on cells of different populations. Particular disclosed examples are analysis of normal versus malignant cells, or a comparison of differential protein expression in cells that are progressing from normal to malignant. The protein content of the microdissected cells may be analyzed using techniques such as immunoassays, 1D and 2D gel electrophoresis characterization, Western blotting, liquid chromatography quadrupole ion trap electrospray (LCQ-MS), Matrix Assisted Laser Desorption Ionization/Time of Flight (MALDI/TOF), and Surface Enhanced Laser Desorption Ionization Spectroscopy (SELDI). In addition to permitting direct comparison of qualitative and quantitative protein content of tumor cells and normal cells from the same tissue sample, the methods also allow for investigation of protein characteristics of tumor cells, such as binding ability and amino acid sequence, and differential expression of proteins in particular cell populations in response to drug treatment. The present methods also provide, through the use of protein fingerprinting, a rapid and reliable way to identify the source tissue of a tumor metastasis.